

REMARKS

Upon entry of the foregoing amendment, claims 23-43 will be pending in the instant application. Claims 1-22 and 44 have been canceled.

The Office Action includes rejections under 35 U.S.C. §§ 102(b), 103(a), and 112, second paragraph, as well as under the judicially created doctrine of obviousness-type double patenting. In view of the remarks to follow, Applicants request that these rejections be reconsidered and withdrawn.

Obvious-Type Double Patenting

Claims 1-14 and 17-43 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claim 9 of commonly owned U.S. Patent No. 5,852,188 to Cook (“the Cook patent”). Applicants respectfully traverse this rejection.

An obviousness-type double patenting rejection is “analogous to [a failure to meet] the non-obvious requirement of 35 U.S.C. § 103” except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 U.S.P.Q. 29 (CCPA 1967); MPEP § 804 at 800-22. The analysis employed in an obviousness-type double patenting rejection must satisfy the same standards applicable to a rejection under § 103, except that only the claims of the earlier patent (rather than the disclosure) may be used as prior art. *In re Braat*, 937 F.2d 589, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991); *In re Vogel*, 422 F.2d 438, 441-42 (C.C.P.A. 1970); MPEP § 804 at 800-22. Such analysis requires, among other

things, a determination of the scope and content of the pertinent prior art and an identification of the differences between it and the claims at issue. *Specialty Composites v. Cabot Corp.*, 845 F.2d 981, 989, 991 (Fed. Cir. 1988). Moreover, to establish a *prima facie* case of obviousness, “there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant.” *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998).

Significantly, the Office Action fails to provide any evidence or technical reasoning indicating that those of ordinary skill in the art would have been motivated to modify the teachings provided by claim 9 of the Cook patent, much less modify its teachings in a way that would have produced a claimed invention. For example, the present claims are directed to *gapped* oligomeric compounds comprising a plurality of covalently-bound nucleosides wherein *an internal region linked by chiral Rp phosphorothioate 2'-deoxynucleosides is flanked by two external regions of the recited formula*. By contrast, claim 9 of the Cook patent does not specify such a structure. Rather, claim 9, which depends from claims 1 and 2, recites:

An oligonucleotide comprising a plurality of nucleoside units linked together via phosphate linkages, wherein:

at least one of the nucleoside units is a non-naturally occurring nucleoside unit; and

at least two of the nucleoside units are linked via chiral phosphate linkages (**from claim 1**),

wherein said chiral phosphate linkages are selected from the group consisting of chiral Sp phosphorothioate, chiral Rp phosphorothioate, chiral Sp alkylphosphonate, chiral Rp alkylphosphonate, chiral Sp phosphoamidate, chiral Rp phosphoamidate, chiral Sp chiral phosphotriester or chiral Rp phosphotriester (**from claim 2**); and

wherein the oligonucleotide forms at least a portion of a preselected RNA or DNA sequence (**from claim 9**).

Thus, claim 9 makes no mention of the claimed *gapped* oligomeric compounds. Although the claim requires that at least two of the nucleoside units be “linked via chiral phosphate linkages,” it does not teach or suggest that such linkages link 2'-deoxynucleosides, or that the chiral phosphate linkages be located in an internal region.

Moreover, there is no evidence of record indicating that those skilled in the art would have been motivated to modify the subject matter of claim 9 of the Cook patent in a way that would have produced one of Applicants’ claimed gapped oligonucleotide compounds. In view of these deficiencies, Applicants respectfully request the rejection based upon obviousness-type double patenting be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-22 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Although Applicants respectfully traverse this rejection, Applicants submit that in view of the foregoing amendments, this rejection is now moot. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102(b)

1. *U.S. Patent No. 5,883,237 to Stec et al. (“the Stec patent”)*

Claims 1-4, 7, 8, 11-13, and 17-43 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by the Stec patent. Applicants respectfully traverse this rejection because the Stec patent does not disclose each and every element of the claimed inventions.

Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ.2d 1051, 1053 (Fed. Cir. 1987) (“A

claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.”).

Applicants’ claimed inventions relate to *gapped* oligomeric compounds (“gapmers”) that have, *inter alia*, an internal chiral Rp deoxypyrophorothioate region flanked on each end by external regions

The compounds disclosed in the Stec patent, in contrast, do not have an internal region of Rp chiral phosphorothioate linked 2'-deoxynucleosides and two external flanking regions. In fact, the Stec patent does not disclose oligonucleotides having three regions as defined by Applicants’ claims. Rather, the Stec patent merely discloses solid phase synthesis of a polymer having a predetermined sequence of R_p or S_p linkages (*see, e.g.*, col. 2, lines 56-61). Nowhere does the Stec patent teach an oligonucleotide having *3 regions*: (1) an internal region of R_p chiral phosphorothioate linkages as defined in Applicants’ claims; and (2) & (3) two external regions, as defined in Applicants’ claims, flanking the internal region. Column 7, lines 14-67 of the Stec patent confirms this: the only sequences disclosed in the cited passage of the Stec patent are either all “ps,” all “pr,” or alternating “ps” and “pr” linkages (col. 7 at lines 41-43). Indeed, any assignment of three regions within any of the oligonucleotides within the cited disclosure of the Stec patent would be completely arbitrary and would not comport with Applicants’ claimed inventions.¹ The Stec patent, therefore, does not disclose every element of Applicants’ claimed inventions. Accordingly, reconsideration and withdrawal of the rejection based upon the Stec patent is respectfully requested.

¹ The Office Action appears to maintain the rejection over the Stec patent by improperly citing to Applicants’ *specification* in view of the Stec patent, rather than Applicants’ claims. A

2. *U.S. Patent No. 5,506,212 to Hoke et al. ("the Hoke patent")*

Claims 1-4, 6-8, 11-13, and 17-43 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by the Hoke patent. Applicants respectfully traverse this rejection because the Hoke patent does not disclose each and every claim element.

As noted above, the claims relate to gapped oligomeric compounds having an internal region of chiral Rp phosphorothioate-linked 2'-deoxynucleosides and two external flanking regions (*see, e.g.*, claim 23). Although the Office Action asserts that claims 2 and 4 of the Hoke patent teaches the recited characteristic at columns 7-9 and claims 2 and 4 (Office Action at 3), Applicants cannot find any such teaching in the Hoke patent. Claim 2 of the Hoke patent, for example, recites an oligonucleotide represented by sequence I.D. No. 4, wherein at least 75% of the nucleoside units are joined together by Rp phosphorothioate 3' to 5' linkages. Significantly, nowhere in claim 2, or the remainder of the Hoke patent, does Hoke teach that claim 2 describes Applicants' claimed an internal region of Rp chiral phosphorothioate-linked 2'-deoxynucleosides and two external regions *flanking* said internal region. Applicants do not understand (and the Office Action does not explain) how the phrase "at least 75% of the nucleoside units are joined together by R_p phosphorothioate 3' to 5' linkages" amounts to a disclosure of Applicants' claimed oligomers having the three specified regions. Accordingly, reconsideration and withdrawal of the reject based upon the Hoke patent is respectfully requested.

3. *U.S. Patent No. 5,852,188 to Cook ("the Cook patent")*

proper § 102 rejection, however, should be based upon Applicants' claims alone and *not*

Claims 1-14 and 17-43 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by the Cook patent. Applicants respectfully traverse this rejection because the Cook patent does not disclose each and every claim element.² The Cook patent, for example, does not disclose an internal region of Rp chiral phosphorothioate linked 2'-deoxynucleosides and two external regions flanking said internal region. Although the Office Action asserts that the Cook patent teaches the recited characteristic at column 5, line 45 to column 7 (Office Action at 3-4), Applicants note that no such teaching is present in the Cook patent. Rather, the Cook patent discloses sequence-specific oligonucleotides having either *substantially pure* or *pure* chiral Sp phosphorothioate, chiral Rp phosphorothioate, chiral Sp alkylphosphonate, chiral Rp alkylphosphonate, chiral Sp phosphoamidate, chiral Rp phosphoamidate, chiral Sp phosphotriester, and chiral Rp phosphotriester linkages (*see, e.g.*, col. 5, lines 46-67).

The Office Action at page 4 relies on Applicants' *specification* for the purported teaching at page 27, lines 30-35, that "any compound [can be] connected to either side of the chiral phosphorothioate." However, *no such teaching* appears at page 27, lines 30-35, nor is it seen how such would be relevant to the instant rejection even if it did

Although the Office Action attempts to arbitrarily define internal and external regions within the oligonucleotides disclosed in the Cook patent for the purpose of alleging that such regions correspond to those recited in Applicants' claims, the Cook patent simply does not disclose the claimed structure. The Office Action, for example, has not even indicated where

Applicants' specification.

² Although the instant rejection is a rejection under 35 U.S.C. § 102(b), the Cook patent is *not* available as prior art against the instant application under 35 U.S.C. § 102(b). In particular, the instant application has a filing date of November 12, 1999, whereas the Cook patent became

the transitions lie between the alleged internal and external regions of the oligonucleotides disclosed in the Cook patent. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) based upon the Cook patent is respectfully requested.

Rejection Under 35 U.S.C. § 103

Claims 1-4, 6-14, 17-21, and 24-42 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Cook patent in combination with U.S. Patent No. 5,532,130 to Alul (“the Alul patent”). Applicants respectfully request that this rejection be withdrawn, as there is no evidence of record indicating that those of ordinary skill would have been motivated to combine the teachings of the Cook and the Alul patents or even that such combination would have resulted in one of Applicants’ claimed inventions. As discussed above for example, the Cook patent does not disclose “an internal region of Rp chiral phosphorothioate linked 2'-deoxynucleosides and two external regions flanking said internal region” as recited by Applicants’ claims. The Alul patent does not remedy this deficiency, nor has it been alleged to do so. Thus, combination of the Cook and Alul patents would not have resulted in any claimed inventionAccordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) are respectfully requested.

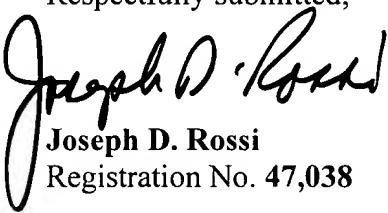
available to the public on December 12, 1998, less than one year before the instant application

Conclusion

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Applicants respectfully submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested.

Respectfully submitted,



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was filed. Accordingly, the Cook patent is not a 35 U.S.C. § 102(b) reference.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend the application as follows:

In the Claims:

Please cancel claims 1-22 and 44, without prejudice to their presentation in a continuing patent application.